The epidemiologic features of thrombotic brain infarction have been studied in comparison with myocardial infarction over a 12-year period in over 5,000 men and women. Results are reported with respect to sex ratio and incidence, type of infarction, and various other aspects.

# VASCULAR DISEASE OF THE BRAIN—EPIDEMIOLOGIC ASPECTS: THE FRAMINGHAM STUDY

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THE importance of vascular disease of the brain as a cause of death and disability hardly requires emphasis. It is the third leading cause of death in this country.1 The bulk of vascular disease of the brain, however, is part of a larger problem of cardiovascular disease including hypertensive cardiovascular disease and coronary heart disease. As an aggregate, these vascular diseases are responsible for more than half the deaths in this country. With an increasing proportion of the population reaching advanced age, vascular disease of the brain will assume even greater importance. Because of the importance of these diseases as contemporary health problems, an explosive expansion of research into the causes, pathogenetic mechanism, and possible modes of prevention has taken place.

A study of the epidemiologic features of a disease, i.e., the circumstances under which it arises and flourishes, often holds the key to its prevention. Epidemiologic information reflecting on factors which relate to the incidence of "stroke" is, however, scarce and incomplete. From an investigation of the personal traits, habits, and environment

of those who have developed a stroke in comparison to those who have remained free of it, it is possible to identify highly susceptible individuals and to determine the factors which appear to predispose to "stroke." Such a study is being carried out in Framingham, Mass., in respondents of a random sample of adult men and women.

The purpose of this report is to determine the incidence of the various types of "stroke" in a general population of adults, and to detail in what particulars those who developed vascular accidents of the brain differed from those who did not. Since there is no reason to believe the epidemiologic features of all types of stroke are the same, attributes of the population under observation were examined in relation to the development of each of the major types of stroke.

Among the major types of vascular accident of the brain, thrombotic infarction (i.e., "cerebral thrombosis") appears to be the most solidly established as related to atherosclerosis. For this reason, attention has been focused on the epidemiologic features of non-embolic infarction of the brain which

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will be compared with myocardial infarction, another consequence of atherosclerosis. Such a comparison should provide clues to pathogenesis, a better understanding of the natural history of these diseases, and have preventive and therapeutic implications.

#### Methods

Recognizing the growing importance of the cardiovascular diseases as a force of morbidity and mortality in the United States of America, the National Heart Institute established a field study in Framingham, Mass. to investigate the epidemiology of coronary heart disease and hypertensive cardiovascular disease. Since 1949 this investigation into the host and environmental factors related to development of these diseases has been in continuous operation, biennially examining a selected sample of the adult population of this town.

The derivation of the population sample being investigated is detailed in Table 1. From a random sample of 3,074 men and 3,433 women aged 30-62 vears, living in the town, it was possible to obtain the cooperation of about 70 per cent. To these 4,469 respondents a group of 740 volunteers within the same age range was added after analysis revealed the same distribution of personal attributes pertinent to the investigation.2-5 After exclusion of those persons with any manifestation of coronary heart disease on the initial examination. it was possible to undertake a study of 5,127 adults free of the disease. This group has been observed biennally to determine in what particulars persons who developed coronary heart disease under observation differed from those who remained free of the disease. As a result, factors associated with an excess incidence of the disease have been identified.6-9

Since thrombotic brain infarction, like coronary heart disease, is believed

Table 1—Derivation of Framingham Study Population

	Total	Men	Women
Random sample	6507	3074	3433
Respondents	4469	2024	2445
Volunteers	740	312	428
Respondents free			
of CHD	4393	1975	2418
Volunteers free	=0.4	00=	400
of CHD	734	307	427
Total free of CHD	5127	2282	2845
Total free of CHD and CVA	5106	2270	2836

to be on an atherosclerotic basis, it appeared reasonable to determine if the same factors were associated with an excess rate of development of each of these diseases. Accordingly, all subjects who displayed any neurological stigmata suggesting vascular disease of the brain were also excluded from the population at risk leaving 5,106 men and women free of both coronary heart disease and vascular disease of the central nervous system (Table 1). Data are now available covering 12 years of observation.

Subjects have been examined at twoyear intervals in a clinic manned by National Heart Institute personnel, and especially set up for purposes of an epidemiologic investigation. The details of the clinical examination, sampling procedure, laboratory methods, and criteria for the diagnosis of coronary heart disease have been published previously.<sup>2-11</sup> In addition to, or in place of, this detailed cardiovascular examination, when subjects missed an examination, systematic collection of data from hospital records, medical examiners' reports, death certificates, and physicians' reports have been routinely obtained.

Follow-up of the population sample under investigation has been reasonably complete with less than one per cent "lost" over a decade of follow-up. As a result of all the information obtained from close medical surveillance, it is unlikely that more than a small number of episodes either of coronary heart disease or cerebrovascular accident have escaped detection in this general population sample.

## Criteria for Diagnosis

The minimal criteria employed for the diagnosis of myocardial infarction included new development of unequivocal electrocardiographic evidence of myocardial infarction or serum enzyme evidence of muscle necrosis in an appropriate clinical setting. In cases lacking a history, the development of a definite electrocardiographic pattern of myocardial infarction since the previous tracing was accepted as evidence of an unrecognized myocardial infarction. All new cases suspected of having sustained a myocardial infarction were examined by two independent observers and the case later jointly reviewed by the whole staff making use of the entire clinical and hospital records.

The diagnosis of overt vascular discase of the brain was based on the occurrence of a "stroke." Minimal criteria for a nonhemorrhagic "stroke" consisted of the sudden onset of a localizing neurologic deficit, such as hemiparesis, aphasia, homonymous hemianopia, among others. A diagnosis of "stroke" due to hemorrhage was made in the presence of change in the state of consciousness, headache, and signs of meningeal irritation in association with a bloody spinal fluid under increased pressure, whether with (usually intracerebral hemorrhage) or without (usually subarachnoid hemorrhage) other localizing neurological deficits. A diagnosis of embolus to the brain was made if a source for embolus (i.e., atrial fibrillation, rheumatic heart disease with mitral stenosis, recent myocardial infarction) was present, the clinical course consistent (i.e., rapid onset and clearing, slightly bloody spinal fluid, a more localized deficit), or the occurrence of associated peripheral emboli elsewhere noted. Hospital and clinic protocols were reviewed by a neurologist (M.E.C.), and the professional staff of the study. Independent assessments of the type of "stroke" by the consultant neurologist and the clinic staff were in good agreement.

The blood pressure, cardiac status and serum lipid levels were held back from the reviewers and the differential diagnosis was made independent of these findings.

Among those who died, 43 per cent had postmortem examination; in two-thirds of these the brain was examined. Angiograms were obtained in the majority of subjects suspected of subarachnoid hemorrhage. Lumbar punctures were obtained in a high percentage of all strokes and in every case suspected of a brain hemorrhage.

The rates of development of initial myocardial infarction and vascular disease of the brain, over 12 years of observation, in subjects classified according to the presence and level of certain attributes under investigation, were determined. The "risk" (probability) of developing each disease was expressed as the ratio of the number of observed myocardial infarctions or "strokes" to what would be expected for the particular subgroup under scrutiny, considering its age and sex composition and disregarding other attributes. The expected number of events was determined by applying the age specific disease rates (in five-year intervals) noted in the whole population in each sex, to the age-sex composition of each subgroup under consideration. The ratio was multiplied by 100 to obtain a whole number which is termed the "morbidity ratio." This ratio adjusts for any possible differences in age and sex composi-

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tion in the various subgroups under consideration when the variable being studied is related to either age or sex.

The population was stratified according to the level of each of the following attributes: serum cholesterol, blood pressure, relative body weight, vital capacity, cigarette smoking habit, electrocardiographic abnormalities, cardiac enlargement by x-ray, among others. The rate of development of initial thrombotic brain infarctions and myocardial infarctions was then determined over the next 12 years according to the level of these personal attributes on the initial examination. For purposes of analysis, no attempt has been made to take into account any possible changes in these attributes during the period of observation.

In the population initially free of vascular disease of the brain 110 persons developed some difficulties which demanded their consideration as possible stroke victims. Of these, 90 met the established criteria.

#### Results

In 12 years of observation of 5,106 men and women aged 30-62 years, examined and found to be initially free of both coronary heart disease and vascular disease of the brain, 57 instances of thrombotic brain infarction occurred. 27 in men and 30 in women. These were subjected to detailed scrutiny. In the same 12-year period there were also four hemorrhages arising within the brain, 16 hemorrhages arising in the subarachnoid space, and 13 brain infarctions due to embolus (Table 2). Atherosclerotic brain infarction was by far the most common type of "stroke." accounting for 63 per cent. Subarachnoid hemorrhage (18 per cent) and embolus to the brain (15 per cent) were the next most common types, far exceeding hemorrhage into the brain substance (4 per cent) in frequency.

Table 2—Relative Frequency of Various Types of Cerebrovascular Lesions in 12 Years, Men and Women 30-62\* at Entry

Type	Men	Women	Both	% of Total
Thrombotic brain infarction	27	30	57	63
Subarachnoid hemorrhage	8	8	16	18
Cerebral embolus	4	9	13	15
Intracerebral hemorrhage	2	2	4	4
Total	41	49	90	100

<sup>\*</sup>Due to small number of persons in the 60-62 age group, all other tabulations are calculated for subjects aged 30-59.

Except possibly for embolism, where there appeared to be a female predominance, no particular type of stroke was peculiar to either sex.

In this population, followed for this length of time, the average age at occurrence of subarachnoid hemorrhage (56 years) was below that for thrombosis (59 years) or intrabrain hemorrhage (62 years). Strokes before age 50 were almost invariably due to embolus or subarachnoid hemorrhage.

In 12 years of observation of this population sample, concurrence of new diagnoses of coronary heart disease, intermittent claudication, and thrombotic brain infarction was noted at about double the expected frequency of such coincidences. This suggests an underlying disorder common to all these presumed manifestations of atherosclerosis. For this presentation, comparison will be limited to the epidemiologic features of brain and myocardial infarctions.

## Age and Sex

Because there were only two subjects with vascular accidents of the brain over

		Brain	Infarction		Myocardial Infarction		
Men	Pop. at Risk	New Cases	Incidence per 1,000	Pop. at Risk	New Cases	Incidence per 1,000	
30–39	824	2	2.4	825	23	27.9	
40-49	769	9	11.7	770	44	57.1	
50–59	609	15	24.6	617	61	98.9	
Women							
30-39	1,036	1	1.0	1,036	2	1.9	
40-49	952	7	7.4	955	7	7.3	

26.7

Table 3—Incidence of Thrombotic and Myocardial Infarction in 12 Years, Men and Women 30-59 at Entry

age 60 at entry, incidence of thrombotic brain and myocardial infarction was calculated for the age group 30-59 years at entry.

786

21

50-59

The incidence of both myocardial infarction and thrombotic brain infarction quite clearly increased with age in both sexes. However, while in women the incidence of the two manifestations of atherosclerosis was almost identical at all ages, in men the incidence of brain infarction lagged 20 years behind that of infarction of the myocardium (Table 3). In myocardial infarction a marked male predominance was noted. No predominance of either sex was observed in thrombotic infarction of the brain.

#### Serum Cholesterol Level

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While an association of serum cholesterol level with the rate of development of coronary heart disease is well-established, 6,12-15 the relation of serum lipids to development of vascular disease of the brain has been controversial.

20

25.3

For the entire age range under observation, in both men and women, classified according to the level of cholesterol in the blood, only a modest excess of brain infarctions occurred in subjects with "elevated" (260 mg or greater) serum cholesterol levels. This was not statistically significant (Table 4). In myocardial infarction, for the

Table 4—Occurrence of Thrombotic	<b>Brain Infarction</b>	in 12 Years	According to Serum
Cholesterol Level, Men and Women	30-59 at Entry		

Initial Serum			N	lew Cases	Developi	ng in 12	Years	_
Cholesterol Pop. at Level (mg %) Risk	Pop. at	30-49			50–59			30–59
	Obs.	Exp.	M. R.*	Obs.	Exp.	M. R.	M. R.	
<220	2,218	4	8.2	49	14	11.0	127	94
220–259	1,482	7	6.2	112	7	11.4	61	79
260 +	1,037	8	3.7	217	14	12.0	117	140

<sup>\*</sup>The rising trend (slope) is significantly different from zero at the 0.05 level. Serum cholesterols were not obtained on all persons in the study group.

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Table 5—Occurrence of Myocardial Infarction in 12 Years According to Serum Cholesterol Level, Men and Women 30-59 at Entry

T-:::-1 C			Ne	ew Cases I	)evelopin	g in 12 Y	ears		
Initial Serum Cholesterol Pop. at		30–49			50–59			30–59	
Level (mg %) Risk	Obs.	Exp.	M. R.*	Obs.	Exp.	M. R.*	M. R.*		
<220	2,226	18	32.8	55	23	29.5	78	66	
220-259	1,490	26	26.4	98	24	25.8	93	96	
260+	1,039	29	13.8	211	33	22.2	149	173	

<sup>\*</sup>The rising trend (slope) is significantly different from zero at the 0.05 level. Serum cholesterols were not obtained on all persons in the study group.

entire age range under study, a clear-cut relationship was demonstrated, but this was less evident in older subjects, particularly among the women (Table 5).

Examination of the occurrence of thrombotic strokes in men and women initially under age 50, when the serum cholesterol was determined, revealed an upward trend in the incidence of strokes the higher the serum cholesterol level (Table 4). Despite small numbers, the trend was statistically significant in this younger age group.

#### **Blood Pressure**

The firmly established clinical observation of a relation between hypertension and "stroke" was confirmed. The

entire study group was classified on the initial examination into three blood pressure categories: "normotensive" (less than 140/90); "hypertensive" (160 and/or 95 or greater); and "borderline" (all others). "Hypertension" appeared to increase the probability of developing a thrombotic brain infarction about fivefold over that experienced by "normotensives" (Table 6). Risk of myocardial infarction was also increased in "hypertensives."

## **Electrocardiographic Abnormalities**

Electrocardiographic abnormalities of left ventricular hypertrophy intraventricular block, and persistent nonspecific S-T and T wave abnormalities have all

Table 6-Occurrence of Thrombotic Brain and Myocardial Infarction in 12 Years According to Hypertensive Status, Men and Women 30-59 at Entry

Initial		New Cases Developing in 12 Years								
Hypertensive Status†	B	rain Infar	Мус	Myocardial Infarction						
	Obs.	Exp.	M. R.*	Obs.	Exp.	M. R.*				
Normotensive	9	20.6	44	37	63.5	58				
Borderline	15	21.0	71	72	59.1	122				
Hypertensive	31	13.4	232	48	34.4	140				

<sup>\*</sup> The rising trend (slope) is significantly different from zero at the 0.05 level.
† Normotensive—All blood pressures <140/90
Hypertensive—All blood pressures >160 and/or/95
Borderline—All not normotensive or hypertensive

Table 7-Occurrence of Thrombotic Brain and Myocardial Infarction in 12 Years According to Electrocardiographic Abnormality, Men and Women 30-59 at Entry

F.C.C	New Cases Developing in 12 Years							
E. C. G. Abnormality† Initial Examination	Bı	ain Infar	ction	Myocardial Infarction				
	Obs.	Exp.	M. R.*	Obs.	Exp.	M. R.		
Absent	38	50.8	75	137	144.6	95		
Present	17	4.2	408	20	12.4	161		

<sup>\*</sup> The rising trend (slope) is significantly different from zero at the 0.05 level.

been shown to be associated with an excess development of coronary heart disease.6-8 The presence of these antecedent electrocardiographic abnormalities, or enlargement of the heart on x-ray, was even more strikingly related to the rate of development of thrombotic "stroke" than myocardial infarction (Tables 7 and 8).

## Vital Capacity

A low vital capacity appeared to be associated with excess development of both thrombotic brain and myocardial infarction (Table 9). More data will have to be accumulated before the relationship to brain infarction can be established with statistical assurance. In subjects who also had enlarged hearts, electrocardiographic impairments, this could reflect diminished myocardial reserve. Such subjects with combinations of these findings had an extremely high risk of developing a stroke.

## Obesity

No relation between the degree of obesity (comparing subjects 20 per cent above median weight for their height and sex and those below this relative weight) and either thrombotic brain or myocardial infarction could be demonstrated (Table 10). Overweight was, however, strikingly related to development of angina pectoris and sudden death from coronary heart disease.

## Cigarette Smoking

The cigarette smoking habit was associated with excess development of myocardial infarction in both men and women. In thrombotic brain infarction, a trend was apparent in men, with a higher incidence of strokes developing, the greater the number of cigarettes smoked daily. In women, there were too few heavy smokers to test the relationship with the small numbers of cases

Table 8—Occurrence of Thrombotic Brain Infarction in 12 Years According to Heart Enlargement by X-Ray, Men and Women 30-59 at Entry

GCE or LVH†	New Cases Developing in 12 Years					
Initial	В	rain Infa	rction			
Examination	Obs.	Exp.	M. R.*			
Absent	35	43.4	81			
Present	20	11.3	177			

<sup>\*</sup>The rising trend (slope) is significantly different from zero at the 0.05 level. † GCE—generalized cardiac enlargement. LVH—left ventricular hypertrophy.

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IVH—left ventricular hypertrophy (definite or doubtful).

IVB—intraventricular block (definite or doubtful).

NSA—nonspecific S-T and T-wave abnormality (definite).

Table 9—Occurrence of Thrombotic Brain and Myocardial Infarction in 12 Years According to Vital Capacity, Men and Women 30-59 at Entry

				New C	ases Devel	oping in	12 Years		
Initial Vital			Bı	rain Infar	ction	Myo	Myocardial Infarction		
Capacity	M	F	Obs.	Exp.	M. R.	Obs.	Exp.	M. R.*	
Low	<3.0	<2.0	14	9.1	154	30	23.8	126	
Medium	3.0-3.9	2.0-2.9	31	33.6	92	92	87.6	105	
High	4.0+	3.0+	10	11.5	87	33	44.0	75	

<sup>\*</sup> The trend (slope) is significantly different from zero at the 0.05 level. Vital capacity levels were not obtained on all persons in the study group.

available for analysis. For men (Table 11), although a trend is apparent, the numbers are small and do not establish a statistically significant association between cigarette smoking and thrombotic brain infarction. Further observation will be necessary before any conclusion can be made regarding this relationship.

#### Combined Abnormalities

Subjects with various combinations of "abnormalities," shown to be associated with an excess rate of development of thrombotic brain infarction, appeared to be highly susceptible to development of a stroke (Table 12). Thus, persons with two or more abnormalities (i.e., hypertension, "elevated" serum cholesterol level, electrocardiographic abnormalities) ran a high risk of developing

a thrombotic stroke. This was also true for subjects with combinations of two or more abnormalities associated with excess risk, including cardiac enlargement and a low vital capacity as well as electrocardiographic abnormalities.

### Discussion

In general, factors which appear to predispose to development of myocardial infarction, evidently also increase susceptibility to thrombotic infarction of the brain. Persons at high risk of one clinical manifestation of atherosclerosis appeared to be highly susceptible to other manifestations as well.

Certain notable differences in the epidemiology of myocardial and brain infarctions are, however, apparent. While a marked male predominance exists in

Table 10-Occurrence of Thrombotic Brain and Myocardial Infarction in 12 Years According to Framingham Relative Weight, Men and Women 30-59 at Entry

		New C	ases Devel	oping in	12 Years	
Initial F. R. W.*	Bı	ain Infar	Myocardial Infarction			
	Obs.	Exp.	M. R.	Obs.	Exp.	M. R.
<120	46	46.5	99	136	138.7	98
120 +	9	8.2	110	20	17.4	115

<sup>\*</sup> F.R.W. = Each person's actual weight was related to a median weight for each height group for each sex, multiplied by 100.

Framingham Relative Weight was not available for all persons in the study group.

Table 11-Occurrence of Thrombotic Brain and Myocardial Infarction in 12 Years According to Cigarette Smoking Status, Men 30-59 at Entry

Cigarette Smoking Status Initial Examination	New Cases Developing in 12 Years						
	Bı	ain Infar	ction	Myocardial Infarction			
	Obs.	Exp.	M. R.	Obs.	Exp.	M. R.*	
Nonsmoker	5	10.0	50	31	48.6	64	
"Heavy" smoker†	8	4.8	166	31	24.4	127	

The rising trend (slope) is significantly different from zero at the 0.05 level.

† >1 package/day.

incidence of myocardial infarction, no predominance of either sex was noted for brain infarction. In this regard brain infarction more closely resembles one other manifestation of coronary heart disease, angina pectoris. The incidence of angina pectoris is also virtually identical in the two sexes.6

Hemorrhage into the brain was much less common than reported in hospital series or autopsy data. Hospital data and autopsy studies may tend to overestimate the prevalence of brain hemorrhage since the case fatality rate is in excess of 90 per cent, and the condition of the patient serious enough almost always to warrant hospitalization.

A preventive approach to the control of vascular disease of the brain seems imperative. There is little hope of reversing damage to the brain once an

infarction has occurred, and a small lesion can produce extensive disability. Only about one-third of those developing thrombotic brain infarctions had any "prodromal symptoms" which would have allowed some attempt to prevent a full blown "stroke."

While myocardial infarctions curred quite regularly in subjects who were apparently in good health, it was uncommon for thrombotic "strokes" to occur unheralded by illness. In three of every four subjects developing a thrombotic stroke, there were antecedent findings of a major cardiovascular disorder. These subjects had evidence of hypertensive cardiovascular disease, coronary disease, congestive heart failure, or intermittent claudication, for which most were receiving some form of treatment.

Table 12-Occurrence of Thrombotic Brain and Myocardial Infarction in 12 Years According to Specified Abnormalities,† Men and Women 30-59 at Entry

No. of Abnormalities	New Cases Developing in 12 Years					
	Brain Infarction			Myocardial Infarction		
	Obs.	Exp.	M. R.*	Obs.	Exp.	M. R.*
None	10	26.2	38	54	82.2	66
One only	23	20.6	112	70	54.8	128
Two or more	22	7.1	309	28	15.3	191

<sup>\*</sup> The rising trend (slope) is significantly different from zero at the 0.05 level. † Cholesterol >250, "Hypertension" (160 and/or/95), ECG-LVH, IVB, NST. Subjects lacking one or more measurements are not included in this tabulation.

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The finding of an even more striking relation of cardiac impairment, such as x-ray enlargement and electrocardiographic abnormalities to "stroke" than to myocardial infarction, is of interest. It suggests a direct contribution of impairment of myocardial function in precipitating a "stroke" in subjects predisposed by hypertension and an elevated serum cholesterol level. This suggestion is further supported by the finding of a high prevalence of congestive heart failure among those who developed strokes. Also those with a combination of electrocardiographic abnormalities, cardiac enlargement on x-ray, and a low vital capacity (a combination of findings strongly suggesting myocardial insufficiency) had an extremely high probability of developing a stroke, as did those with evidence of hypertensive cardiovascular disease with cardiac enlargement. This suggests that cardiac impairment contributes to development of stroke over and above its indication of the poor condition of the vasculature.

Thrombotic brain infarctions carried a case fatality rate of about 15 per cent in the acute stage, and among survivors were distressingly often (50 per cent) severe enough to cause some permanent disability.

Once a stroke occurs, the immediate outcome appears to depend more on the location and kind of lesion than any other factors. Also, after the patient survives the acute stage, prognosis with respect to disability and rehabilitation mostly depends upon the rapidity with which signs of spontaneous improvement appear.

Once the victim survives the acute stage, he may survive a surprisingly long time, particularly if no associated serious cardiac disease is present. This can cause a considerable drain on the resources of the patient, his family, and the community. In those with associated medical illnesses, the length of survival

very much appears to depend upon the course of the associated cardiovascular disease.

It seems clear that a preventive approach, requiring early identification of unusually susceptible individuals, will more likely result in a decline in morbidity and mortality from vascular disease of the brain than does further improvement in therapy.

It seems reasonable that measures which appear appropriate for the prevention of coronary heart disease may also be effective in the prevention of thrombotic brain infarction, the most common type of "stroke." If the medical profession is going to strive to prolong life, it must try to make certain that a disabling "stroke" will not be the reward for achieving advanced age.

## Summary

The epidemiologic features of thrombotic brain infarction in comparison to myocardial infarction, another presumed manifestation of atherosclerosis, have been investigated in 5,106 men and women aged 30-62 years, examined, and found to be free of both coronary heart disease and vascular disease of the brain.

In 12 years of observation, 167 myocardial infarctions and 57 thrombotic brain infarctions occurred. In men, but not women, the incidence of brain infarction lagged 20 years behind that of myocardial infarction.

Thrombotic brain infarction was by far the most common type of "stroke," accounting for 63 per cent of all such events. Hemorrhage into the brain was the least common (4 per cent), but most lethal type of "stroke."

The rate of development of myocardial and brain infarction, according to the level of certain personal attributes measured on the initial examination, was determined. In general, factors which appeared to predispose to development of a myocardial infarction, also increased susceptibility to thrombotic infarction of the brain.

Persons most highly susceptible to development of thrombotic brain infarction would appear to be older aged men and women, ill with cardiovascular disease, with enlarged hearts, electrocardiographic abnormalities, and a low vital capacity; having hypertension, an elevated serum cholesterol level, and possibly given to excessive cigarette smoking. Persons with any two of these could be considered unusually susceptible. The obese, however, ran no excess risk of either stroke or myocardial infarction.

Subjects with evidence of "cardiac impairments," such as electrocardiographic abnormalities, enlargement of the heart on x-ray, and a low vital capacity, were unusually susceptible. An excess prevalence of congestive heart failure was noted in subjects who developed "strokes." This suggests a direct contribution of impairment of cardiac function in precipitating a stroke.

## Conclusions

The sex ratio noted in myocardial infarction differed from that of thrombotic infarction of the brain. While a marked male predominance was noted in myocardial infarction, no predominance of either sex was noted in thrombotic infarction of the brain. In men the incidence of brain infarction lagged 20 years behind that of myocardial infarction, but it was equal in women.

Thrombotic brain infarction was by far the most common type of "stroke" accounting for 63 per cent of all such events. Subarachnoid hemorrhage and embolus to the brain were the next most common types (about 15 per cent), far exceeding the incidence of hemorrhage into the brain, the least common, but most lethal type of stroke which accounted for only 4 per cent of the strokes.

Probability of developing both myocardial and brain infarctions was decidedly increased in subjects who on the initial examination had an elevated blood pressure and serum cholesterol level, and electrocardiographic abnormalities. Excess development of myocardial infarction was noted in cigarette smokers and those with a low vital capacity. While an excess development of thrombotic brain infarction appeared to be associated with cigarette smoking and a low vital capacity, with the numbers available statistically significant differences could not be demonstrated. The obese developed no excess of either myocardial or thrombotic brain infarctions.

Subjects with two or more "abnormalities," shown to be associated with an excess rate of development of thrombotic brain infarction, appeared to be highly susceptible to development of this type of "stroke."

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